IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
	)	
Kenneth C. CUNDY et al.	)	Group Art Unit: 1616
	)	
Application No.: 09/974,768	)	Examiner: Barbara P. Badio
	)	
Filed: October 9, 2001	)	Confirmation No.: 6895
	)	
For: BILE-ACID CONJUGATES FOR PROVIDING SUSTAINED SYSTEMIC CONCENTRATIONS OF DRUGS	)	

RESPONSE TO OFFICE COMMUNICATION

Assistant Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

In complete response to the Office Action of July 16, 2004, Applicants submit the following response.

In the Office Action, the Examiner sets forth a Restriction Requirement among eight (8) **exemplary** groups of claims.

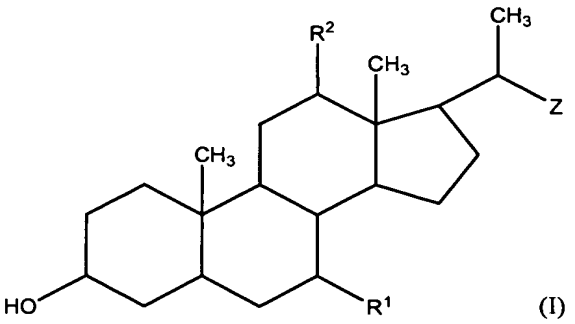
Initially, Applicants would like to thank the Examiner for discussing the outstanding Restriction Requirement with Applicants' representative via telephone on Friday, August 13, 2004. During the phone conversation, the Examiner confirmed that the groups as set forth in the Restriction Requirement were **exemplary.** The Examiner noted that because the groups are exemplary, Applicants may define a group for examination not set forth among those specified in the Office Action.

In addition, Applicants believe that in paragraph 3 (page 6, Office Action dated 7/16/04), the Examiner is requiring Applicants to elect a single disclosed species from under the elected Group for search purposes.

Applicants respectfully traverse the restriction requirement as set forth in the Office Action, and thus, expressly reserve the right to Petition the Commissioner requesting removal thereof. Nevertheless, in order to comply with the requirements of 37 C.F.R. § 1.143, Applicants indicate below a provisional election of a group for examination and one species within the elected Group for purposes of searching.

In accordance with the groups as set forth being **exemplary** and, thus, not limiting, Applicants hereby propose and elect the following group for examination:

Elected Group: Claims 1, 3, 4, 6, 8, 9, and 23 (in part) drawn to compounds of formula (I) and compositions thereof:



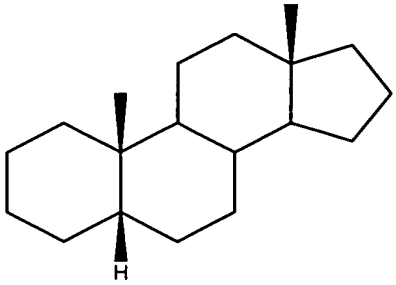
(I)

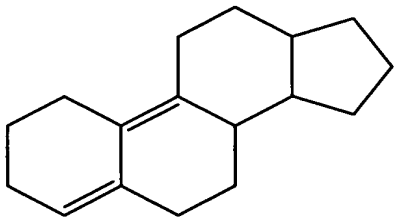
wherein:

R^1 and R^2 are independently hydrogen or hydroxy;

Z is a group $-M-Q^{x'}$, wherein M is $-CH_2CH_2C(O)-$ and $Q^{x'}$ is a group derived from a linear oligopeptide comprising a first moiety D' and further comprising from 1 to 3 amino acids, wherein $Q^{x'}$ is of the formula $-I'_i-J'_j-D'-K'_k-R^{40'}$ wherein I', J', and K' are independently selected from naturally occurring α-amino acid moieties; i, j, and k are independently 0 or 1, where at least one of i, j, and k is 1; and D' is a drug containing at least one carboxylic acid group and at least one moiety selected from the group consisting of a primary amino group, a secondary amino group or a hydroxyl group, with the provisos that the drug is not a GABA analog; L-Dopa, an L-aromatic amino acid decarboxylase inhibitor, a catechol O-methyl transferase inhibitor or derivatives thereof; a naturally occurring α-amino acid or an ester or carboxamide of a naturally occurring α-amino acid; a polypeptide derived from a linear oligopeptide containing at least 3 α-amino acids, an oligonucleotide, a cyclophane derivative, a

diethylenetriaminopentaacetate derivative, or paramagnetic ion chelates thereof; 5-de-O-methylsporaricin; a bis-(2-chloroethyl)amine containing nitrogen mustard; an HMG-CoA reductase inhibitor; a proline hydroxylase inhibitor; or a steroid containing the carbon substructures of the following formulae:

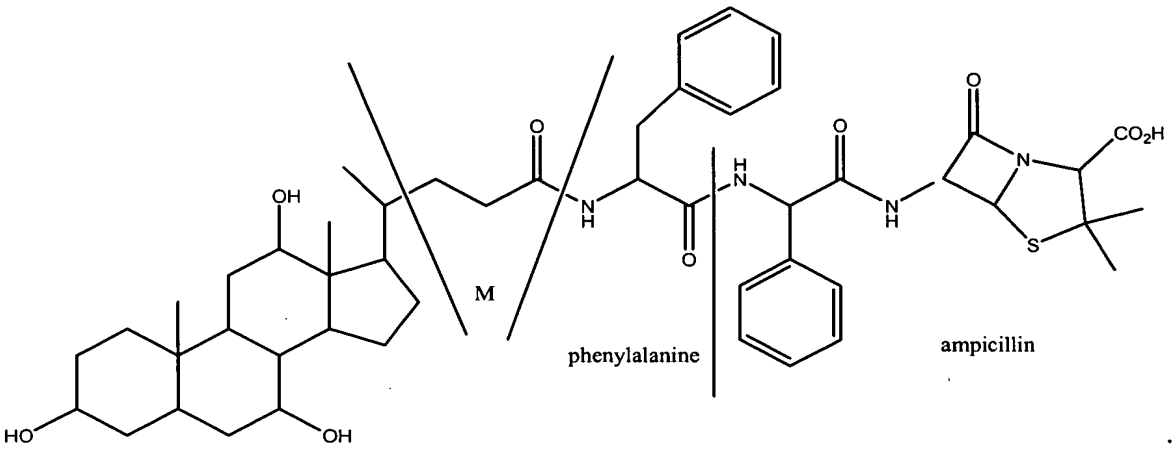




Suitable drugs D' are taught on page 35, line 23 – page 37, line 11. I', J', and K' being derived from a naturally occurring α-amino acid is taught, for example, on page 17, lines 18 – 19.

Applicants respectfully submit that the structure of D' is not the inventive aspect of the claimed compounds. The claimed compounds use the bile acid transport system to provide sustained systemic concentration of orally delivered drugs (D'). The compounds of the proposed group all comprise a bile acid moiety, as illustrated above, linked to a drug (D'). Applicants submit that the precise structure of the drug is not critical and is not the patentable aspect of the claimed compounds. Rather, for the above-elected group, the patentable portion of the compounds of formula (I) is that portion of the compounds up to D'. Accordingly, as discussed during the telephone conversation, with the above-elected group Applicants are willing for the Examiner to search the defined structure of the claimed compounds independent of the structure of D' (*i.e.*, search the compounds of formula (I) as defined in the elected group up to D'), and for the proposed elected group, Applicants will argue patentability based on the defined structure independent of the structure of D'.

With regard to the election of species, Applicants maintain their previous election, with traverse, of the following compound of formula I, for the purposes of searching:



In the elected compound of formula I, X, R^1, and R^2 are hydroxy; Z is a group of the formula -M-$Q^{x'}$; M is $-CH_2CH_2C(O)-$; $Q^{x'}$ is of the structure $-A^{x'}-D'$; $A^{x'}$ is derived from an α-amino acid; and D' is a drug (as disclosed on page 82, lines 13-20). Alpha amino acids are taught on page 33, line 18 – page 34, line 2 and on page 35, lines 1-7). On page 35, line 6, phenylalanine is specifically disclosed as a suitable α-amino acid and phenylalanine is illustrated as a suitable α-amino acid in Figure 4. Suitable drugs D' are taught on page 35, line 23 – page 37, line 11. Ampicillin is specifically disclosed as a suitable drug D' on page 36, line 15.

Applicants note that in the Examiner-Initiated Interview Summary mailed September 29, 2003, Supervisory Patent Examiner Thurman K. Page indicated that Applicants' election of this compound would be considered proper by the U.S. Patent and Trademark Office.

Traversal of Restriction Requirement as set forth in Office Action

Applicants respectfully traverse the restriction requirement as set forth in the Office Action. Under the statute, if two or more independent and distinct inventions are claimed in one application, the application may be restricted to one of the inventions. 35 U.S.C. § 121, MPEP 802 and 803. In the above Restriction Requirement, the Examiner sets forth eight (8) **exemplary** Groups of claims, wherein the Examiner asserts that each group, in part, defines a set of patentably distinct claims.

However, Applicants respectfully submit that it appears that Groups III and IV and Groups VII and VIII are identical. Accordingly, there appears to be direct overlap among the compounds of Groups III and IV and Groups VII and VIII. Because there is direct overlap among the compounds of the different Groups that the examiner has set forth, Applicants submit that it is an improper restriction requirement. If the Examiner maintains that the Groups III and IV and Groups VII and VIII are not identical, Applicants respectfully request that the Examiner point out how Group III differs from Group IV and how Group VII differs from Group VIII.

Moreover, Applicants submit that it is improper for the Office to refuse to examine that which Applicants regard as their invention unless the subject matter of the claims lacks unity of invention. Specifically, in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978), the court articulated the general proposition that:

> [A]n applicant has a right to have *each* claim examined on the merits. If an applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications. Such action would not affect the right of the applicant eventually to have each of the claims examined in the form he considers to best define his invention. If, however, a single claim is required to be divided up and presented in several applications, that claim would never be considered on its merits. The totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim. Further, since the subgenera would be defined by the examiner rather than by the applicant, it is not inconceivable that a number of the fragments would not be described in the specification.

Id. at 331. (Emphasis in original).

In view of the above and similar case law, the Patent Office has set forth a general policy regarding restriction of Markush-type claims in MPEP 803.02. According to the general policy as articulated in the MPEP, "since the decisions in *In re Weber*, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and *In re Haas*, 580 F.2d 461, 198 USPQ 334, it is ***improper*** for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. *In re Harnish*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984)." (MPEP 803.02, emphasis added). Unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature.

Applicants respectfully submit that their proposed elected group for examination clearly exhibits unity of invention. With regard to a common utility, the compounds of proposed elected

group use the bile acid transport system to provide sustained systemic concentration of orally delivered drugs (D'). With regard to a substantial structural feature, the compounds of the proposed elected group comprise a bile acid moiety, as illustrated above, linked to a drug (D'). As discussed above, the precise structure of the drug (D') is not critical, and Applicants are willing for the Examiner to search the defined structure of the compounds independent of the structure of D' (i.e., search the compounds of formula (I) as defined in the proposed elected group up to D'). Therefore, Applicants respectfully submit that the compounds of the proposed elected group clearly evidence unity of invention.

In view of the proposed elected group and the policy regarding restriction of Markush-type claims as provided above, Applicants submit that it is improper for the Office to refuse to examine the proposed elected group since the presently claimed subject matter clearly evidences unity of invention.

Applicants further respectfully submit the compounds of the proposed elected group are so closely related that a search and examination of the entire claim can be made without serious burden. Applicants note that a proper search can be made of the common backbone, as illustrated and discussed above. Applicants submit that any nominal burden placed upon the Examiner to search accordingly to determine the art relevant to Applicants' overall invention is significantly outweighed by the public's interest in not having to obtain and study a vast number of separate patents in order to have available all of the issued patent claims covering Applicants' invention. If the restriction requirement is maintained as the Examiner has proposed, the alternative is to proceed with the filing of hundreds of applications, each consisting of generally the same disclosure, and each being subjected to essentially the same search. This process would place an unnecessary burden on both the Patent and Trademark Office and on the Applicants.

As there appears to be overlap among the compounds of the Groups as set forth by the Examiner, Applicants submit that the restriction requirement is improper. In addition, for the proposed elected group, it would be improper for the Office to refuse to examine that which Applicants regard as their invention when unity of invention exists. Accordingly, Applicants request reconsideration and withdrawal of restriction in view of their proposed elected group.

Conclusion

It is believed that claims Claims 1, 3, 4, 6, 8, 9, and 23 are readable upon the elected species as defined above. Applicants have no intention of abandoning any non-elected subject matter and expressly reserve the right to file one or more continuation and/or divisional applications directed to the non-elected subject matter.

Applicants respectfully submit that their proposed a group for examination clearly evidences unity of invention. Applicants specifically reserve their right under 37 C.F.R.§ 1.144 to petition the Commissioner from the present requirement for restriction if it is made final and from any further dissection by the Examiner of the Markush groups of the compounds of formula I.

In view of the foregoing remarks and proposed elected group, reconsideration of the claims is earnestly solicited. The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

By_____
Deborah H. Yellin
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Dated: August 16, 2004

Patent
Attorney Docket No. 033053-040

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Mail Stop Amendment

In re Patent Application of
Kenneth C. Cundy et al.

Application No.: 09/974,768
Filing Date: October 9, 2001

Group Art Unit: 1616
Examiner: BARBARA P BADIO
Confirmation No.: 6895

Title: BILE-ACID CONJUGATES FOR PROVIDING SUSTAINED SYSTEMIC CONCENTRATIUONS OF DRUGS

AMENDMENT/REPLY TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Enclosed is a reply for the above-identified patent application.

☐ A Petition for Extension of Time is also enclosed.

☐ Terminal Disclaimer(s) and the ☐ $55.00 (2814) ☐ $110.00 (1814) fee per Disclaimer due under 37 C.F.R. § 1.20(d) are also enclosed.

☐ Also enclosed is/are _____

☐ Small entity status is hereby claimed.

☐ Applicant(s) requests continued examination under 37 C.F.R. § 1.114 and enclose the ☐ $385.00 (2801) ☐ $770.00 (1801) fee due under 37 C.F.R. § 1.17(e).

☐ Applicant(s) requests that any previously unentered after final amendments not be entered. Continued examination is requested based on the enclosed documents identified above.

☐ Applicant(s) previously submitted _____
on _____,
for which continued examination is requested.

☐ Applicant(s) requests suspension of action by the Office until at least _____, which does not exceed three months from the filing of this RCE, in accordance with 37 C.F.R. § 1.103(c). The required fee under 37 C.F.R. § 1.17(i) is enclosed.

☐ A Request for Entry and Consideration of Submission under 37 C.F.R. § 1.129(a) (1809/2809) is also enclosed.

☒ No additional claim fee is required.

☐ An additional claim fee is required, and is calculated as shown below.

AMENDED CLAIMS					
	No. of Claims	**Highest No. of Claims Previously Paid For**	**Extra Claims**	**Rate**	**Additional Fee**
Total Claims	23	MINUS 23 =	0	x $18.00 (1202) =	$ 0.00
Independent Claims	3	MINUS 3 =	0	x $86.00 (1201) =	$ 0.00
If Amendment adds multiple dependent claims, add $290.00 (1203)					
Total Claim Amendment Fee					$ 0.00
☐ Small Entity Status claimed - subtract 50% of Total Claim Amendment Fee					$ 0.00
TOTAL ADDITIONAL CLAIM FEE DUE FOR THIS AMENDMENT					**$ 0.00**

☐ A check in the amount of _____ is enclosed for the fee due.

☐ Charge _____ to Deposit Account No. 02-4800.

☐ Charge _____ to credit card. Form PTO-2038 is attached.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17, 1.20(d) and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

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Date: August 16, 2004